Use of the QTc interval and QTc dispersion in patients on haemodialysis: assessment of reproducibility

Sir,

Cardiac arrhythmias, frequently encountered in haemodialysis (HD) patients [1], are one of the major causes of cardiac death in end-stage renal disease (ESRD). Increased QT and QT dispersion (QTd) measurements on a surface electrocardiogram (ECG) have shown to be a useful and reliable means for predicting susceptibility to life threatening ventricular arrhythmias. QT interval, reflecting the total ventricular recovery time, and QTd, a direct measure of regional heterogeneity of myocardial repolarization, are both abnormally prolonged in ESRD [2]. Moreover, recently, these electrical markers were found to be independent predictors of total and cardiovascular mortality in both non-uraemic and uraemic populations [3,4]. In the present study we assessed for the first time the reproducibility of such important marker measurements, for defining and evaluating arrhythmia risk, in HD patients.

A 12-lead-standard ECG, in which all leads were recorded simultaneously (Quinton Q710, Bothell WA, USA), was obtained in 36 patients, 24 males and 12 females, aged 63.5±12.7 years. In 19 out of these 36 patients, a second ECG recording was performed after 12-15 days and a third one after 1 year. At each time point, laboratory parameters, including serum ionized calcium (iCa), potassium (K) and magnesium (Mg) were determined. At the start and end of the study, non-invasive measurements of cardiac index (CI), using electric bioimpedance (CDI Corp, Irvine, CA, USA), were also obtained. On all occasions, ECG recordings, CI and laboratory test measurements were obtained just before the beginning of the first midweek HD session and at the same shift for the individual patient. During the entire study period, no patient was taking potentially QT-prolonging agents or developed serious hypocalcaemia (iCa<0.98 mmol/l) or hyperkalaemia (K>6.3 mmol/l), factors known to cause QT prolongation. The same observer, blinded to the patient’s dataset, analysed all ECG records. QT interval was measured, as reported elsewhere [4], and QTd was defined as the difference between the maximum and minimum QT interval in any two leads. QT intervals and QTd were correlated with different demographic, clinical, laboratory variables and CI. The reproducibility of the ECG indices was assessed with repeated measures analysis of variance (ANOVA) and the intra-individual coefficient of variation (CVi).

First, we assessed the intra-observer variability in QTc and QTdc measurements. Baseline ECG traces of 15 patients were analysed by a single observer on two different occasions. There were no significant differences between the first and second reading: −0.2±4.3 ms for QTc and −1.57±3.3 ms for QTdc. The CVi values of QTc and QTdc were 0.46±0.39 and 4.6±2.4%, respectively. In the whole group of patients (n=36), multivariate analysis identified left ventricular (LV) hypertrophy, defined by Cornell voltage criteria, a low CI, age and time on HD as independent predictors of QTc prolongation (multiple R²=0.46; P<0.01). Both QTd (r=0.385) and QTdc (r=0.365) correlated significantly (P<0.05) only with age.

The results of the reproducibility of the ECG indices in 19 HD patients are shown in Table 1. ANOVA revealed that, unlike the three repeated measurements of QT and QTc, which were comparable, there were significant (P<0.05) differences between the corresponding measurements of QTd and QTdc. Both the short-term (12-15 days) and long-term (1 year) intra-individual variability of the QT and QTc measurements, as assessed by CVi, were quite low, whereas the corresponding variability of both QTd and QTdc measurements were high and unacceptably high, respectively. Changes in QTd and QTdc between baseline and 12-15 days as well as 1 year were independent of the corresponding changes in biochemical parameters, LV mass and CI (Table 1), findings indicating that the observed QTd and QTdc variations were not due to biological variations, at least to those related to ion balances and cardiac structure and function as well. Despite these results, the possibility that the changes in QTd and QTdc measurements over the entire study period were real, most likely due to corresponding changes in cardiac factors not studied here, cannot be excluded.

Our data confirm the results of comparative studies in healthy subjects [5], which showed that the reproducibility of the QT interval was far superior (P<0.01) to that of QTd. Given the marked technical and biological variability of QTc interval, the latter being even more pronounced in the HD setting [2], the finding of an intra-individual variability of QTc as low as 2.7% over a 1-year period is rather surprising and if confirmed in future studies, its implications would be of great clinical value. Previous investigations in non-dialysis patients [6] have shown decreased QT and QTdc with regression of LV mass, after anti-hypertensive treatment, thus raising the possibility that an altered QTc, owing to its...
high reproducibility, may serve as a modifiable risk factor in ESRD. Moreover, proper monitoring of a highly reproducible QTc interval in ESRD patients receiving potentially QT-prolonging medications [7] may be of help to identify small yet perhaps clinically significant changes in ventricular repolarization, and consequently, minimize or prevent drug-induced arrhythmias.

In summary, we showed that the QTc interval, an easily measurable parameter, which has the advantage of not requiring patient cooperation, is highly reproducible in the HD setting. For this reason, it may be used to assess changes in ventricular recovery times due to therapeutic interventions or changes in the underlying disease process. In contrast, QTdc measurements were characterized by a high degree of variability over time. Identifying the sources of variation in QTdc measurements, most likely cardiac in origin, is critical in establishing the credibility and reliability in QTc dispersion required to be used in defining and assessing cardiac risk.

Conflict of interest statement. None declared.

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